REMARKS

Applicants thank the Examiner for the personal interview of July 23, 2008, during which proposed claim changes were discussed, and for agreeing to rejoin the sequence of SEQ ID NO: 1 should the claims be allowed.

After entry of this amendment, claims 1-4, 8-14, and 18-36 are pending, of which claims 18 and 30 are withdrawn. The claims have been amended without prejudice or disclaimer and find support *inter alia* in the original claims. Claims 1 and 13 find further support in the specification at page 6, lines 38-48, and page 7, lines 23-26. Claim 13 finds further support at page 26, lines 35-37. New claims 31-36 have been added and find support *inter alia* in the original claims. New claims 31-35 find further support throughout the specification, for example, at page 5, line 10, through page 6, line 21, and page 6, line 38, through page 8, line 2. New claim 36 finds further support at page 7, lines 23-26. No new matter has been added.

Because SEQ ID NO: 1 (429 bp) is a shorter version of SEQ ID NO: 2 (836 bp), Applicants respectfully request rejoinder of SEQ ID NO: 1 should the claims be found allowable. The present amendment and following remarks address the rejections made in the Office Action dated July 9, 2008.

Claim Rejections – 35 USC § 112

Claims 1-4, 8-14 and 19-29 are rejected under 35 U.S.C. § 112, first paragraph, for lack of an enabling disclosure and for allegedly failing to comply with the written description requirement. Applicants respectfully disagree and traverse the rejections.

Enablement Rejection

The Examiner rejects the claims for lack of enablement, alleging that the specification is only enabled for the promoter sequence of SEQ ID NO: 2. Applicants respectfully disagree. However, in order to expedite prosecution, the claims have been amended without prejudice or disclaimer to recite the regulatory sequence with more specificity. Particularly, the claims as now amended are drawn to the use of the nucleotide sequence of SEQ ID NO: 2, a fragment thereof, or a nucleotide sequence having at least 98% identity to SEQ ID NO: 2 in one expression cassette for directing expression of two nucleic acid sequences in a bi-directional manner. Applicants respectfully request reconsideration in light of the amendment and for the

following reasons.

The Examiner alleges that the specification does not provide guidance for any sequences, or fragments of sequences, other than the full-length sequence of SEQ ID NO: 1 or 2. The Examiner argues that the function of promoter fragments and sequence variants in transgenic plants and deletion analysis of promoters is unpredictable, citing Kim *et al.* (hereinafter "Kim") and Donald *et al.* (hereinafter "Donald"), respectively. The Examiner further alleges that the function of promoter fragments and sequence variants in transgenic plants is unpredictable when the promoter function is regulated by conditional elements, citing Dolferus *et al.* (hereinafter "Dolferus"). The Examiner concludes that undue experimentation would be required to develop and evaluate all promoter-effective molecules that would give bi-directional expression in plants as claimed. It is respectfully submitted that Kim, Donald, and Dolferus do not support the position alleged by the Examiner. Rather, these references support enablement and show that the essential promoter elements occupy only a small fraction of a promoter sequence, which in turn implies that the vast majority of a promoter sequence may be modified or deleted without affecting promoter activity.

Specifically, the Examiner argues that Kim shows that mutation of a single nucleotide significantly altered the strength of expression, while deletions in other regions of the promoter completely eliminated function. However, Kim actually supports enablement. The mutation described in Kim was not a random mutation of a promoter sequence, but a mutational analysis of an essential part of 30 nucleotides of the *nos* promoter (page 106 and 107, first paragraphs right column). This short nucleotide sequence selected by Kim contains two hexamer motifs surrounding a spacer region of 8 nucleotides (page 108, Table 1). By replacing this essential part with mutated oligomers (page 107, full right column) Kim demonstrated the importance of the two hexamer sequence elements. Kim thus found that promoters consist of essential elements which can readily be identified with the help of deletion experiments in combination with a standard search for sequence motifs. The symmetric structure of the hexamers identified by Kim is readily visualized by a person skilled in the art. A symmetric structure consisting of a spacer region surrounded by hexamers or palindromes can be identified by pure sequence analysis with or without the help of computer algorithms. Furthermore, Kim supports the view that even in these sequence elements mutations do not necessarily abolish promoter activity. To the contrary,

Kim shows that only 20 nucleotides out of 30 identified by deletion analysis are important for promoter activity. Kim also shows that mutations in the 20 nucleotides left, like changing one hexamer of the sequence to a palindrome, does improve promoter activity. Changing the spacer region to a symmetric sequence does improve the promoter activity even further (page 110, Table 3, *nos,* 128-CG and *ocs*). Thus Kim discloses that a 30 base pair element can be narrowed down to 20 nucleotides, of which 10 can be mutated, loosing promoter activity only in two constructs. Thus Kim has demonstrated that even in this small element of 30 base pairs, shown to be essential for promoter activity, more than 30% of the bases can be mutated without loosing the activity.

The Examiner cites Donald to support the allegation that promoter deletion analysis is unpredictable. Rather Donald defined a 196 bp long fragment of the *Arabidopsis thaliana* rbc8-1A promoter as being essential and sufficient for promoter activity (page 1717, abstract). Donald also showed that this promoter fragment had the capacity to direct expression independent of its orientation and relative position in the *Adh* promoter. Further sequence analysis showed that this promoter fragment contained further promoter elements necessary for its activity (page 1717 abstract and page 1720, Figure 3). Donald also disclosed that the expression pattern of the promoter fragment can be influenced by other active promoter fragments and enhancing elements contained in the CaMV promoter fragment and the *Adh* promoter used by Donald (page 1724, last paragraph). This does not show that promoter deletion analysis is unpredictable. Rather Donald showed that active fragments and elements from other promoters could restore activity following mutations in essential boxes (see abstract and page 1724). Donald also demonstrated that a promoter fragment identified by deletion analysis can be used independent of its orientation and relative position and still preserve its activity, as long as particular sequence elements like the G-, I- or GT-box are not destroyed by mutation (page 1724, last paragraph). Those boxes have a size of only 12 to 14 base pairs (page 1720, Figure 3) and represent only a minor part of the rbcS-1A LRE sequence of 196 base pairs. Moreover, as in Kim, the mutations described in Donald were site-specific mutations in conserved sequences and not random mutations (see abstract).

Dolferus discloses a detailed analysis of an inducible promoter of about 1 kb in length from *Arabidopsis*. By using only 5 deletion constructs, Dolferus showed that the promoter

contained four different regions (regions I, II, Ill and IV), of which region I was responsible for preventing noninduced expression. Region II contained a positive regulatory element necessary for high level expression. Regions III and IV were the most critical regions for promoter activity. These two regions contained five small promoter elements (page 1075, abstract). Further mutational analysis of these small promoter elements, having a size between 7 and 28 base pairs, showed that only four of them were necessary for preserving promoter activity (page 1085, Figure 6). Dolferus by a simple sequence analysis identified critical regions of the promoter which when mutated affected promoter activity. Analogous to the disclosure of Kim and Donald, the mutations done by Dolferus were not random. This strategy is clearly stated by Dolferus "Site-specific mutagenesis (Kunkel et al., 1987) was used to introduce mutations at four specific regions of the CADH fragment. . . ." (page 1076, first quarter of right column). Dolferus did not show any data of mutations in regions outside the identified sequence elements, but that mutations in essential regions affected promoter activity. Thus, Dolferus demonstrated through simple deletion experiments, in combination with a search for known or predicted promoter boxes, that a person of skill in the art could identify which regions or elements of the promoter are essential for preserving function and any mutations in the essential elements would affect activity.

All three references cited by the Examiner show that promoter fragments with a particular activity can be identified by standard deletion experiments, that essential sequence elements can be predicted and identified by sequence analysis, and that those sequence elements represent only a minor part of the promoter sequence. By showing which parts of the promoter sequence are essential through routine experimentation and that only small parts of the original promoter sequence are necessary for activity, Kim, Donald, and Dolferus demonstrate which parts of a promoter sequence can be changed, which substitutions can and cannot be made which will affect activity, and that the majority of a promoter sequence might be changed without losing promoter activity. This is further in consistent with the Board's finding in *Ex parte Heck* (Appeal No. 2008-2875, copy of the decision attached), where two of the three references, Kim and Donald, were used to show the unpredictability of the promoter art in a nonenablement rejection. As stated by the Board at page 6 of the attached copy of the decision, "[t]he art cited by the Examiner demonstrates the routine nature of promoter analysis, since both Donald and Kim use standard methods to determine which sequence elements affect promoter strength and

which elements have no impact."

Furthermore, the present application describes that the delimitation of the promoter sequence to certain essential regulatory regions can be carried out through routine search and experimentation (see specification at page 7, lines 32-38). Moreover, the specification provides detailed guidance on determining promoter expression and activity, for example at page 5, lines 20-46, and page 21, lines 34-37. The specification provides detailed guidance on cloning the promoters of the invention into a vector as exemplified in Examples 3 and 4, on transformation as in Example 2, and testing for activity as in Examples 5-9. Thus, in view of the working examples disclosed in the specification, one skilled in the art would recognize that screening and testing for promoter activity is routine and is not undue experimentation. The same applies to screening and testing the promoter activity of fragments and variants of the sequences as claimed in the present application, which techniques are also known to one of skill in the art (see Kim, Donald, and Dolferus cited by the Examiner). Again, this is in consistent with the Board's finding in *Ex parte Heck*, where the Board stated "[t]he methods for performing such screening were provided by the specification, and were also well known to those skilled in the art." *See Ex parte Heck*, at page 6 of the attached copy.

Thus, from a promoter sequence and a description of its promoter activity, a person of skill in the art can readily identify promoter fragments and variants with a preserved promoter activity and the important sequence elements contained therein by using routine experimentation as described in the present application and as demonstrated by Kim, Donald, and Dolferus. Furthermore, one of ordinary skill in the art can readily identify the majority of nucleotides in the promoter sequence which are not necessary for activity and which might be changed or deleted without losing the promoter activity. By using routine experimentation, a skilled artisan would be readily able to construct sequence fragments and variants preserving the claimed promoter activity.

In view of the detailed description, guidance, working examples, and high level of skill, the specification enables the full scope of the present claims without undue experimentation. Additionally, even if we are to assume that the amount of experimentation to practice the full scope of the claimed invention might be extensive, as found by the Board in *Ex parte Heck*, such experimentation would have been routine, and not undue experimentation. See *Ex parte Heck*, at

page 6 of the attached copy. Compare, *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988) (routine screening of hybridomas was not "undue experimentation;" the involved experimentation can be considerable, so long as "routine"). On these facts, an analysis under *In re Wands* supports enablement.

For these reasons and in light of the amendments, reconsideration and withdrawal of this rejection is respectfully urged.

Written Description Rejection

The Examiner alleges that the specification only describes SEQ ID NO: 1 or 2 but the specification does not provide a description of any other sequences, or fragments of sequences, for use as promoters. The Examiner further alleges that the specification does not describe which structural features of SEQ ID NO: 2 are critical for function as a promoter. Applicants respectfully disagree. However, to expedite prosecution, the claims have been amended without prejudice or disclaimer to recite the regulatory sequence with more specificity. Applicants respectfully request reconsideration in light of the amendment and for the following reasons.

The "written description" requirement under 35 U.S.C. § 112, first paragraph, serves both to satisfy the inventor's obligation to disclose the technologic knowledge upon which the patent is based, and to demonstrate that the patentee was in possession of the invention that is claimed. *Capon v. Eshhar*, 418 F.3d 1349, 1357, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005); *see also* MPEP § 2163. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. *See* MPEP § 2163 (citation omitted).

A written description of an invention involving a nucleic acid, like a description of a chemical genus, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials. *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993). For a claimed genus, the written description requirement may be satisfied through sufficient description of a representative number of species by actual reduction to practice, by disclosure of relevant identifying characteristics, by functional

characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics. *See Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997). However, the determination of what is required to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter. *Capon v. Eshhar*, 418 F.3d 1349, 1359 (Fed. Cir. 2005).

Here, the specification provides two actual sequences, SEQ ID NOs: 1 and 2. Thus, the structure of the claimed "nucleic acid" is provided. Furthermore, the specification shows, by way of working examples, that the disclosed promoter sequences exhibit the bi-directional expression activity in plants (an actual reduction to practice). Because each embodiment need not be disclosed, the specification provides a representative number of sequences under the standard of *Regents v. Lilly*. See *In re Angstadt*, 537 F.2d 498 (CCPA 1976) (holding that there has never been a requirement that every species encompassed by a claim must be disclosed or exemplified in a working example).

Furthermore, as disclosed in the specification at page 7, lines 32-38, essential regulatory regions in a promoter sequence can be identified with the aid of various computer programs such as the PLACE program or the BIOBASE program. Additionally, as discussed above, the methods for performing screening and testing promoter activity were routine and well known to those skilled in the art. Accordingly, one of ordinary skill in the art could readily identify promoter fragments and variants with a preserved promoter activity from a promoter sequence and a description of its promoter activity by using routine experimentation as described in the present application or known in the art at the time of filing. Because the existing knowledge and content of the art is such that one skilled artisan could readily envision fragments and variants having 98% identity to the disclosed sequences from the present specification, the written description requirement is satisfied. This is also in consistent with the Board's finding in *Ex parte Heck*, where the written description requirement was found to be satisfied for a claim reciting a genus to polynucleotide sequences having at least 98% identity to the single disclosed sequence because "the skilled artisan would know the structure, i.e. at least 98% identity to SEQ

ID NO: 1, as well as the function, having promoter activity." *See Ex parte Heck*, at page 4 of the attached copy.

For at least the above reasons, reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections – 35 USC § 102(b)

The Examiner rejects claims 1-4, 8-14, and 19-29 under 35 U.S.C. 102(b) as being anticipated by Budworth *et al.* (WO 01/98480, hereinafter "Budworth"). Applicants respectfully disagree and traverse the rejection.

During the interview of July 23, 2008, claim language which might be found allowable was discussed. Accordingly, the claims have been amended without prejudice or disclaimer to specify that the regulatory sequence has the bi-directional activity. As discussed during the interview, although Budworth discloses SEQ ID NO: 315 that exhibits 99% sequence identity with SEQ ID NO: 2, Budworth does not teach that SEQ ID NO: 315 has the bi-directional expression activity and does not teach an expression cassette containing SEQ ID NO: 315 in such manner that SEQ ID NO: 315 is located in between two nucleotide sequences so to direct expression of these two sequences in one single cell. Accordingly, it is respectfully submitted that Budworth does not anticipate the present claims because Budworth does not disclose all the limitations of the claims.

In light of the amendments, reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

For at least the above reasons, Applicants respectfully request withdrawal of the rejections and allowance of the claims. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the number given below.

Accompanying this response is a petition for a two-month extension of time to and including December 9, 2008 to respond to the Office Action mailed July 9, 2008 with the required fee payment. No further fees are believed due. If any additional fee is due, the Director is hereby authorized to charge our Deposit Account No. 03-2775, under Order No. 13173-00022-US from which the undersigned is authorized to draw.

Respectfully submitted,

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Attachment: *Ex parte Heck*, Appeal No. 2008-2875, 2008 WL 4266205 (BPAI, Sept. 16, 2008).

2008 WL 4266205 (Bd.Pat.App. & Interf.)

Board of Patent Appeals and Interferences
Patent and Trademark Office (P.T.O.)

Ex Parte Gregory R. Heck, Marianne Malven, James D. Masucci, and Jinsong You

Appeal 2008-2875
Application 10/925,392 Technology Center 1600

Decided: September 16, 2008

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Before DONALD E. ADAMS, LORA M. GREEN, and JEFFREY N. FREDMAN
Administrative Patent Judges
GREEN
Administrative Patent Judge

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the Examiner's final rejection of claims 1, 3-12 and 19.[FN1] We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF THE CASE

The "invention relates to the field of plant molecular biology and plant genetic engineering and polynucleotide molecules useful for the expression of transgenes in plants." (Spec. 1.)

The claims are directed to an isolated polynucleotide having gene regulatory activity, as well as DNA constructs containing the polynucleotide, and transgenic plants transformed with the DNA construct. Claims 1 and 3 are representative of the claims on appeal, and read as follows:

1. An isolated polynucleotide molecule having gene regulatory activity and comprising a sequence selected from the group consisting of a polynucleotide sequence comprising at least 1000 contiguous bases of the polynucleotide sequence of SEQ ID NO: 1 and a polynucleotide sequence comprising at least 98% identity to the polynucleotide sequence of SEQ ID NO: 1.

3. The isolated polynucleotide molecule according to claim 1, wherein said isolated polynucleotide molecule comprises a polynucleotide sequence which exhibits at least about 98% identity with the polynucleotide sequence of SEQ ID NO: 1.

We reverse.

ISSUE (Indefiniteness)

The Examiner contends that the phrase "at least about" renders claim 3 indefinite.

Appellants contend that the Examiner has misinterpreted the claim.

Thus, the issue on appeal is: Is the Examiner's interpretation of claim 3 correct such that the use of the phrase "at least about" renders claim 3 indefinite?

FINDINGS OF FACT
FF1 The Examiner rejects claim 3 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Appellants regard as the invention (Ans. 5).

FF2 The Examiner asserts, citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1218 (Fed. Cir. 1991), that the phrase "at least about" renders the claim indefinite (Ans. 5).

PRINCIPLES OF LAW
Claims are in compliance with 35 U.S.C. § 112, second paragraph, if "the claims, read in light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits." *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385 (Fed. Cir. 1987). However, "breadth is not to be equated with indefiniteness." *In re Miller*, 441 F.2d 689, 693 (CCPA 1971); *see also In re Hyatt*, 708 F.2d 712, 714-15, (Fed. Cir. 1983).

Moreover, under 35 U.S.C. § 112, third paragraph, a "claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers."

ANALYSIS
In *Amgen*, the Federal Circuit found "at least about" to be indefinite given the use of the term "about" coupled with the amount of error inherent in the assay for measurement of specific activity, as well as the fact that there was close prior art. *Amgen*, 927 F.2d at 1218. The court cautioned that the holding "should not be understood as ruling out any and all uses" of "about," as "[i]t may be acceptable in appropriate fact situations." *Id.*

Claim 3 is dependent from claim 1, and thus incorporates all of the limitations of claim 1, thus further limiting it. Claim 1 is drawn to "an isolated polynucleotide molecule" wherein the molecule is selected from the Markush group of either "a sequence selected from the group consisting of a polynucleotide sequence comprising at least 1000 contiguous

bases of the polynucleotide sequence of SEQ ID NO: 1" or "a polynucleotide sequence comprising at least 98% identity to the polynucleotide sequence of SEQ ID NO: 1." As claim 3 recites that the polynucleotide molecule "comprises a polynucleotide sequence which exhibits at least about 98% identity with the polynucleotide sequence of SEQ ID NO: 1," it cannot further limit the second member of the Markush group, *i.e.*, "a polynucleotide sequence comprising at least 98% identity to the polynucleotide sequence of SEQ ID NO: 1," as it would in fact broaden the breadth of that member of the Markush group. Thus, it must modify the first member of the Markush group, that is "a sequence selected from the group consisting of a polynucleotide sequence comprising at least 1000 contiguous bases of the polynucleotide sequence of SEQ ID NO: 1." The polynucleotide molecule of claim 3 therefore must comprise at least 1000 contiguous bases of the polynucleotide sequence of SEQ ID NO: 1 as well as being at least about 98% identical with the polynucleotide sequence of SEQ ID NO: 1 (*see also* Reply Br. 17). As sequence identity can be precisely determined, and the fact that the polynucleotide molecule of claim 3 must comprise at least 1000 contiguous bases of the polynucleotide sequence of SEQ ID NO: 1, we find that the skilled artisan would understand the meets and bounds of claim 3.

CONCLUSIONS OF LAW
Thus, we conclude that claim 3 is definite under 35 U.S.C. § 112, second paragraph, and the rejection is reversed.

ISSUE (WRITTEN DEESCRIPTION)

The Examiner contends that claims 1, 3-12, and 19 do not comply with the written description requirement of 35 U.S.C. § 112, first paragraph, as the genus encompassed by the claims is very large (Ans. 6).

Appellants contend that the Specification supports that Appellants were in possession of the full scope of the invention (App. Br. 9).

Thus, the issue on appeal is: Whether the disclosure as filed demonstrates that Appellants were in possession of the subject matter of claims 1, 3-12, and 19?

FINDINGS OF FACT
FF3 Claims 1, 3-12, and 19 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement (Ans. 6).

FF4 The Examiner finds that the "essential feature of the claimed polynucleotide is that it has 'gene regulatory activity.' However, the specification has not provided any specific structures or subsequences that are associated with this essential function." (Ans. 6.)

FF5 The Examiner finds further that the genus of sequences encompassed by the claims is very large, finding that the genus may encompass 7.7×10^{25} or larger molecule (Ans. 6-7).

FF6 Thus, according to the Examiner:

> Given the extremely large genus encompassed by the claims with only one of the species reduced to practice, and given the total lack of any description of a structure/function relationship between certain subsequences of SEQ ID NO:1 and the function of having gene regulatory activity, the requirement for written description

has not been met.
(Ans. 7.)

PRINCIPLES OF LAW
"The burden of showing that the claimed invention is not described in the application rests on the PTO in the first instance." *In re Edwards*, 568 F.2d 1349, 1354 (CCPA 1978). A written description of an invention involving a nucleic acid, like a description of a chemical genus, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials. *Fiers v. Revel*, 984 F.2d 1164, 1171 (Fed. Cir. 1993). While "examples explicitly covering the full scope of the claim language" are not typically required, a sufficient number of representative species must be included "to demonstrate that the [applicants] possesses the full scope of the invention." *LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005). However,

> the determination of what is needed to support generic claims to biological subject matter depends on a variety of factors, such as the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, the predictability of the aspect at issue, and other considerations appropriate to the subject matter.

Capon v. Eshhar, 418 F.3d 1349, 1359 (Fed. Cir. 2005).

ANALYSIS
Appellants argue that they "have explicitly taught the structure of the promoter sequences by providing the nucleic acid sequence of SEQ ID NO:1, a sequence provided with the application as filed." (App. Br. 10.) According to Appellants, "[w]hile the claims encompass fragments of the sequence SEQ ID NO:1 and sequences with at least … 98% identity with SEQ ID NO:1, these groups define a subset of sequences fully described by SEQ ID NO:1." (*Id.*)

We agree. Claim 1, the broadest claim on Appeal, recites an "isolated polynucleotide molecule having gene regulatory activity and comprising a sequence selected from the group consisting of a polynucleotide sequence comprising at least 1000 contiguous bases of the polynucleotide sequence of SEQ ID NO: 1 and a polynucleotide sequence comprising at least 98% identity to the polynucleotide sequence of SEQ ID NO: 1." As to "a polynucleotide sequence comprising at least 1000 contiguous bases of the polynucleotide sequence of SEQ ID NO: 1," structure is provided, i.e., 1000 contiguous bases of SEQ ID NO: 1, a sequence that is 2190 nucleotides long, and also knows the function, promoter activity. As to sequences that have "at least 98% identity to the polynucleotide sequence of SEQ ID NO: 1," the same analysis applies, that is, the skilled artisan would know the structure, i.e. at least 98% identity to SEQ ID NO: 1, as well as the function, having promoter activity.

CONCLUSION
Thus, we find that claims 1, 3-12, and 19 comply with the written description requirement of 35 U.S.C. § 112, first paragraph, and the rejection is reversed.

ISSUE (ENABLEMENT)

The Examiner contends that the Specification fails to enable claims 1, 3-12, and 19 as required by 35 U.S.C. § 112, first paragraph.

Appellants contend that the claims are enabled by the Specification (App. Br. 14).

Thus, the issue on Appeal is: does the Specification enable claims 1, 3-12, and 19 as required by 35 U.S.C. § 112, first paragraph?

FINDINGS OF FACT
FF7 The Examiner rejected claims 1, 3-12, and 19 under 35 U.S.C. § 112, first paragraph, on the grounds that "the specification, while being enabling for an isolated polynucleotide molecule comprising SEQ ID NO: 1 and for polynucleotides comprising at least 1000 contiguous bases of SEQ ID NO:1, does not reasonably provide enablement for an isolated polynucleotide molecule comprising a sequence which has at least 98% identity, at least about 98% identity, or at least 99% identity with SEQ ID NO:1." (Ans. 7-8.)

FF8 The Examiner made the following findings with respect to the factors set out in *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).[FN2]

FF9 *The breadth of the claims*: The Examiner notes that claims "1, 3, and 19 are broadly drawn to an isolated polynucleotide molecule having gene regulatory activity and having at least 98% identity, or at least about 98% identity, or at least 99% identity with SEQ ID NO:1." (Ans. 8.)

FF10 *Nature of the invention and the state of the prior art*: The Examiner notes that the "nature of the invention is the construction of a chimeric promoter for use in plants." (Ans. 8.)

FF11 *The amount of direction or guidance presented and the existence of working examples*: According to the Examiner while the Specification teaches that a chimeric promoter, presumably SEQ ID NO:1, was cloned into two different expression vectors to drive expression of two different marker genes, it "has not taught any polynucleotides with 98% identity or 'about' 98% identity or 99% identity to SEQ ID NO:1 that have gene regulatory activity." (Ans. 8-9.)

FF12 *The relative skill of those in the art, the predictability or unpredictability of the art, and the quantity of experimentation necessary*: The Examiner, citing Donald[FN3] and Kim,[FN4] states that the prior art demonstrates "that mutation of promoter sequences produces unpredictable results," and that "[e]ven minor alterations can alter promoter activity." (Ans. 9.)

PRINCIPLES OF LAW
"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application." *In re Wright*, 999 F.2d 1557, 1561-62 (Fed. Cir. 1993).

"[T]o be enabling, the specification … must teach those skilled in the art how to make and use *the full scope of the claimed invention* without 'undue experimentation.'" *Id.* at 1561, (emphasis added), *quoted in Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997). Thus, "there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed." *In re Vaeck*, 947 F.2d 488, 496 & n. 23

(Fed. Cir. 1991), *quoted in* Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 1374 (Fed. Cir. 1999). Some experimentation, even a considerable amount, is not "undue" if, e.g., it is merely routine, or if the specification provides a reasonable amount of guidance as to the direction in which the experimentation should proceed. *See* In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

ANALYSIS
The Examiner concludes:

> In the absence of this guidance, one skilled in the art is left to randomly produce an endless number of substitutions or deletions of nucleotides from SEQ ID NO:1, and test each new molecule for having gene regulatory activity, which is undue experimentation. Given the breadth of the claims encompassing any polynucleotide have 98% identity, "about" 98% identity, or 99% identity to SEQ ID NO:1, and given unpredictability of the art and lack of guidance of the specification as discussed above, undue experimentation would have been required by one skilled in the art to make and use the claimed invention.

(Ans. 9.)

Appellants argue that it is well within the level of ordinary skill in the art to prepare nucleic acid sequences that are 98% identical to SEQ ID NO: 1 (App. Br. 15). Moreover, the Specification teaches the preparation of derivatives of full length promoter sequences, as well as methods of determining the activity of such promoter sequences (*id.*). As to Kim and Donald, while Appellants acknowledge that the "some deletions and mutations will reduce activity of a promoter," both references "employ standard screening methods to assess the promoter activity of sequences comprising deletions and/or point mutations." (App. Br. 18-19.)

We agree. Even if we were to assume that the amount of experimentation to practice the full scope of the claimed invention might be extensive, such experimentation would have been routine. The art cited by the Examiner demonstrates the routine nature of promoter analysis, since both Donald and Kim use standard methods to determine which sequence elements affect promoter strength and which elements have no impact. The methods for performing such screening were provided by the Specification, and were also well known to those skilled in the art. *See, e.g.*, Johns Hopkins Univ. v. Cellpro, Inc., 152 F.3d 1342, 1360 (Fed. Cir. 1998) ("test [for undue experimentation] is not merely quantitative … if it is merely routine"); *Ex parte* Kubin, 83 USPQ2d 1410, 1416 (Bd. Pat. App. & Int. 2007). Thus, we conclude the Specification provides an enabling disclosure.

CONCLUSIONS OF LAW
We thus conclude that the Specification enables claims 1, 3-12, and 19 as required by 35 U.S.C. § 112, first paragraph, and the rejection is reversed.

ISSUE (Anticipation)

The Examiner contends that polynucleotide molecule of claim 3 is anticipated by Brevario.[FN5]

Appellants contend that "because claim 3 is more narrow than claim 1 and claim 1 is acknowledged to define over the art, the rejection is without merit." (Reply Br. 17.)

Therefore, the issue on appeal is: Has the Examiner established that the polynucleotide

molecule of claim 3 is anticipated by the sequence of Brevario?

FINDINGS OF FACT
FF13 Claim 3 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Brevario.

FF14 Claim 3 is dependent from claim 1, but claim 1 was not rejected.

FF15 Brevario is cited for teaching a sequence of a partial tubA2 gene that comprises 93.8% identity with SEQ ID NO: 1 (Ans. 10).

PRINCIPLES OF LAW
In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997).

ANALYSIS
As noted above in the indefiniteness analysis, the polynucleotide molecule of claim 3 must comprise at least 1000 contiguous bases of the polynucleotide sequence of SEQ ID NO: 1 as well as being at least about 98% identical with the polynucleotide sequence of SEQ ID NO: 1. As the Examiner has not made any findings that the sequence of Brevario comprises comprise at least 1000 contiguous bases of the polynucleotide sequence of SEQ ID NO: 1, and apparently does not do so as claim 1 was not included in the rejection, the Examiner has not established that the sequence of Brevario meets all of the limitations of claim 3, and thus has not set forth a prima facie case that Brevario anticipates claim 3.

CONCLUSION
We therefore find that the Examiner has failed to establish that the polynucleotide molecule of claim 3 is anticipated by the sequence of Brevario, and the rejection is reversed.

SUMMARY

Because the Examiner has failed to set forth a prima facie case of patentability as to any of the claims on appeal, all of the rejections on appeal are reversed.

REVERSED

FN1. This appeal was heard on August 13, 2008.

FN2. The factual considerations discussed in *Wands* are: (1) the quantity of experimentation necessary to practice the invention, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

FN3. Donald, "Mutation of either G box or I box sequences profoundly affects expression from the Arabidopsis rbcS-1a promoter," *The EMBO J.*, Vol. 9, pp. 1717-1726 (1990).

FN4. Kim, "A 20 nucleotide upstream element is essential for the nopaline synthase (nos) promoter activity," *Plant Molecular Biology*, Vol. 24, pp. 105-117 (1994).

FN5. Breviaro, GenBank Accession AJ488063 (2002).

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